

REMARKS

The Applicants thank the Examiner for the examination to date and for the withdrawal of the previous rejections. The Applicants respectfully request reconsideration of the present application in view of the foregoing amendments and the reasons that follow.

I. Status of the Claims

While not acquiescing to any grounds of the rejections, independent claims 14 and 20 are amended to remove “or” from “and/or”; support therefor can be found in, *inter alia*, ¶ [0032] of the Specification as published and original claim 3. Claim 20 is further amended to correct for a minor informality. No new matter is introduced and claims 14-20 are currently pending to be examined on their merits.

II. Claim Rejections – 35 U.S.C. § 103

Claims 14-17 and 20 are rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over WO 01/82875 (“Cutie”) in view of US 5,547,683 (“Yano”). Claims 14-17 and 20 are rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over US 2004/0106660 (“Kositprapa”) in view of Yano¹. Claims 14 and 18-20 are rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over US 2003/0060488 (“Sugiyama”) in view of Yano. Claims 14-20 are rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Sugiyama in view of Cutie or Kositprapa and further in view of Yano. The Applicants respectfully traverse all of these rejections.

(i) Present claims are non-obvious over the teachings of Cutie and Yano

Cutie does not teach or suggest every element recited in independent claims 14 and 20. Specifically, as acknowledged by the Office on p. 3 of the Office Action, Cutie does not teach at all the specific coating material as presently claimed – Cutie merely discloses that either the core

¹ The Applicants assume that the rejections with respect to claims 14-17 and 20 as stated on p. 4 of the Office Action are based on Kositprapa in view of Yano, with the latter being inadvertently omitted from the page.

or the first layer of a formulation, or both, may contain two active ingredients, metformin and pioglitazone (Cutie, p. 2, line 31 – p. 3, line 2). Moreover, Cutie does not teach or suggest at all coating a core with an aqueous dispersion of pioglitazone hydrochloride, as recited in present claims 14 and 20. In fact, to the extent that Cutie discloses a coating material, Cutie describes the material as an outer “shell” (e.g., Cutie, p.7, lines 13-17), which is far different from the presently claimed “aqueous dispersion.”

Yano does not remedy these deficiencies. The Office relies on Yano merely because Yano in passing discloses using 5% HPC-SSL for a granule in one example. The Office then goes a step further and concludes that “it would have been obvious ...to substitute the low viscosity cellulosic polymer HPC-SSL or HPC-SL ... with predictable results.” The Applicants respectfully traverse. In fact, the Applicants respectfully submit that the Office’s assertion is based on mere hindsight, and contrary to the Office’s misconstrued teachings of Yano and Cutie, one of ordinary skill in the art would not have a reason to combine the teachings of Yano with those of Cutie.

(A) Cutie and Yano do not teach the viscosities of the presently claimed cellulose

At the outset, present independent claims 14 and 20 as amended now recite two requirements with respect to the viscosity of the cellulose. Nowhere do Yano and Cutie, alone or in combination, teach or suggest these recitations. As described above, to the extent that Yano discloses a cellulose, Yano only mentions a 5% (w/v) solution embodiment, with no description of the viscosity of the solution, and nowhere does it teach or suggest the presently recited viscosity of a 2% (w/v) solution. Viscosity of a solution can be affected by a host of different factors, and thus the viscosity of a solution at a certain concentration without more information is not predictable based on that at a different concentration. Even assuming, *arguendo*, that one can derive the viscosity of the presently recited 5% (w/v) solution from Yano’s teaching, the Office has not shown any evidence that one would reach the presently recited viscosity of a 2% (w/v) solution.

Thus, multiple elements of the claims are not disclosed by the teachings of Cutie and Yano, alone or in combination, and the present claims are thus non-obvious over the teachings of Cutie and Yano, alone or in combination.

(B) No reason to combine the teachings of Cutie and Yano

The Office's assertion that one would reach the predictable results based on combined teachings of Cutie and Yano is based on hindsight that is impermissible under MPEP § 2142. Yano's teachings focus on a method for producing a microgranulated particle to improve the solubility of the particle, and Yano does not at all teach or suggested the presently claimed coated preparations. In fact, Yano's teachings rely on reducing the particle size of the drug uniformly by granulation to improve dissolution and absorption of the drug particle ("...it is necessary to control the granulation to yield a microgranulated particle by..." Yano, col. 6, lines 13-44, bold emphasis added). Namely, the "HPC-SL" and "HPC-SSL" of Yano are used as binders merely to improve handling at granulation and have little to do with improving dissolution, as in the presently claimed preparations. In other words, regardless of the type of the binder, Yano's goal is to reduce the particle size and to make it as uniform as possible ("...particle of not more than 0.2 mm ...and a sharp distribution of particle size" Yano, col. 2, lines 34-51).

By contrast, in the presently claimed preparations, HPC-SL and HPC-SSL are used as coating materials during pioglitazone coating and are selected for the purpose of rapid dissolution of pioglitazone, especially dissolution within the first 15 minutes of the dissolution test (see e.g., ¶ [0010] and Examples in the present published Specification). In stark contrast to Yano's teachings, the presently claimed celluloses are not intended, and do not need to undergo granulation to achieve the rapid dissolution. Such rapid dissolution based on the type of cellulose employed is unexpected based on Yano's teachings that can accomplish its goal via a entirely different process (i.e., granulation). In fact, Yano's teachings could not be expected to manifest the desirable dissolution properties as a result of these specific celluloses. Thus, such unexpected results of the presently claimed preparations rebut any *prima facie* case of

obviousness. Further, the Office's assertion is mere hindsight. *Sanofi-Synthelabo v. Apotex, Inc.*, 550 F.3d 1075, 1088 (holding that the application of hindsight is inappropriate where the prior art does not suggest the properties and advantages).

One of ordinary skill in the art would not have a reason to combine the teachings of Cutie and Yano. As explained above, in order for Yano's teachings to work, it is "necessary" to reduce the size of the particle. Cutie does not even teach or suggest a "particle," let alone require or deem it "necessary" to reduce the size thereof. Specifically, Cutie only teaches a "core," which is to be coated with a solid shell, as opposed to the presently claimed aqueous dispersion. Thus, not only would one of ordinary skill in the art not have had a reason to combine the teachings of Cutie and Yano, but the combined teachings would render moot the purpose of Yano to improve dissolution by reducing particle size. Accordingly, no *prima facie* obviousness is established. MPEP § 2143.01 (V) (stating that if proposed modification would render the prior art invention being modified unsatisfactory for its intended purpose, then there is no suggestion or motivation to make the proposed modification).

Thus, at least in view of the foregoing, the Applicants respectfully submit that one of ordinary skill in the art would not have had a reason to combine the teachings of Cutie and Yano. Even assuming, *arguendo*, that these teachings were combined, any possible case of *prima facie* obviousness would be rebutted by the unexpected results set forth above.

(ii) *Present claims are non-obvious over the teachings of Kositprapa, Cutie, Sugiyama, and/or Yano*

The office's rejections based on Kositprapa in view of Yano and Sugiyama in view of Cutie/Kositprapa further in view of Yano are similar to those with respect to Cutie in view Yano, and the Applicants respectfully traverse the same.

As already explained in the April 24, 2009 reply and as acknowledged by the Office on pp. 5-7, Sugiyama and Kositprapa do not teach and suggest every element recited in the present claims. Specifically, neither of Sugiyama and Kositprapa teaches or suggests the recited aqueous

dispersion that contains the specific cellulose. Similar to the rejection regarding Cutie and Yano, the Office relies on Yano to remedy the deficiencies. However, the Applicants respectfully submit that there is no “synergistic” or “enhanced” effect suggested by any of these teachings (*see* Office Action, p. 9), contrary to the Office’s statement. In fact, similar to the explanation set forth above, one of ordinary skill in the art would not have had a reason to combine the teachings of Yano with those of Sugiyama and/or Kositprapa. Furthermore, even assuming, *arguendo*, that these teachings were combined, any possible case of *prima facie* obviousness would be rebutted by the unexpected results set forth above. Thus, the present claims are non-obvious over the teachings of Kositprapa, Cutie, Sugiyama, and/or Yano.

Therefore, the Applicants respectfully request that the rejections be withdrawn.

CONCLUSIONS

The Applicants believe that the present application is now in condition for allowance and thus respectfully request favorable reconsideration of the application.

The Office is invited to contact the undersigned by telephone if a telephone interview would advance the prosecution of the present application.

The Office is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, the Applicants hereby petition for such extension under 37 C.F.R. § 1.136 and authorize payment of any such extensions fees to Deposit Account No. 19-0741.

Respectfully submitted,

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